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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/350,518 07/09/99 REED

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EXAMINER

HUNT, J

ART UNIT

PAPER NUMBER

1642

8

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.
09/350,518

Applicant(s)

Reed et al.

Examiner
Jennifer Nichols, Nee Hunt

Group Art Unit
1642



☒ Responsive to communication(s) filed on Aug 16, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-16, 18-27, 29-44, and 46-49 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-16, 18-27, 29-44, and 46-49 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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Response to Amendment

Acknowledgment is made of applicant's cancellation of claims 17, 28, and 45. Claims 1-16, 18-27, 29-⁴⁴~~22~~, and 46-49 are pending, and addressed herein.

Specification

The objection to the specification for making contradictory statements is withdrawn in light of applicant's clarification of the record, and declaratory evidence.

The objection to the specification for not clearly stating which isoform of BAG is bound, and which antibody was used in the example embodiments is withdrawn in light of applicant's clarification of the record.

Claim Rejections Withdrawn

1. The rejection of claims 9, 10, 18, and 47 are withdrawn in light of applicant's clarification of the record, and amendments thereto.
2. The rejection of claims 1-11, 13-17, 19-21, 24-28, 32, 34-36, and 42-46 under 35 USC 102(a) as being anticipated by Krajewski et al., and Tang et al. are withdrawn in light of applicant's declarations.
3. The rejection of claims 1-11, 13-17, 19-21, 24-28, 32, 34-36, and 42-46 under 35 USC 103(a) as being anticipated by Krajewski et al., and Tang et al., in view of Sano et al., US Patent

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5,665,539 (March 16, 1999), An et al., 5,882,864 (March 16, 1999), or Ravdin et al., US Patent 5,862,304 (January 19, 1999) are withdrawn in light of applicant's declarations.

Claim Rejections Maintained/New Grounds of Rejection

4. The rejection of claims 16-37 and 44-45 as lacking an enabling disclosure for the full scope of the claimed invention is maintained for reasons of record set forth in the previous office action, and upon further consideration is newly applied to claims 1-15, 38-43, and 46-49.

As set forth in the previous office action, because the specification, while being enabling for detecting increased BAG-1 (*the truncated form taught in Takayama et al., Cancer Research, Vol 38, page 3116, abstract*) as an indicator of increased overall survival or distant metastasis free survival in Stage I or Stage II breast cancer patients, does not reasonably provide enablement for detection of an increase or decrease in any and all BAG gene expressions as an indicator of prognosis, risk of recurrence, risk of metastasis, or monitoring treatment effectiveness for any and all cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the

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prior art, 6) the relative skill of those in the art, 7) the predictability of the unpredictability of the art, and 8) the breadth of the claims (see *Ex parte Forman*, 230 USPQ 546, BPAI, 1986).

The specification discloses that increased levels of BAG-1 gene expression detecting using a monoclonal antibody to the isoform BAG-1 (a truncated form of the full protein) predicts increased overall survival or distant metastasis free survival in patients with Stage I or Stage II breast carcinoma.

The claims recite methods of detection of an increase in any and all BAG gene expressions as an indicator of decreased risk of metastasis or recurrence for any and all cancer. The claims also recite methods of detection of a decrease in BAG gene expressions as an indicator of increased risk of metastasis or recurrence for any and all cancer.

The prior art teaches that in many cancers, increased BAG expression is correlated with poor prognosis and increased risk of distant metastasis and tumor recurrence. *Tang et al.*, *Journal of Clinical Oncology*, Vol 17, No 6, pages 1710-1719, (June 1999) teaches that increased BAG-1 expression was significantly associated with shorter disease free and overall survival in all stages of breast cancer (table 4, page 1718). The results of *Tang et al.* are in direct contradiction with those of the instant application, which illustrates how even minute differences in experimental technique can alter the conclusions drawn from the study. Further, *Zapata et al.*, *Breast Cancer Research and Treatment*, Vol 47, pages 129-140 (1998) teaches that BAG-1 levels are higher in invasive breast cancers (page 138, 1st column, 3rd paragraph). *Yawata et al.*, *Oncogene*, Vol 16, pages 2681-2686 (1998) teaches that increased BAG-1 levels promote

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metastasis in colon cancer (abstract and page 2681, 2nd column, last paragraph). Additionally, *Takaoka et al., Oncogene, Vol 14, pages 2971-2977 (1997)* teaches that over expression of BAG-1 promotes pulmonary metastasis of melanoma (abstract).

Therefor the art teaches that increased levels of BAG expression do not indicate decreased risk of metastasis or recurrence for any and all cancers and likewise that decreased levels of BAG expression do not indicate increased risk of metastasis or recurrence for any and all cancers. Similarly, detection of the different isoforms of BAG have lead to differing conclusions about breast cancer prognosis. Thus because the art sets forth specific examples in which the full scope of the instant claims are not enabled, one of ordinary skill in the art at the time the invention was made would not have been enabled to practice the full scope of the claimed invention.

With regards to claims 16-37 and 44-45, applicant argues that the amendment of the claims to require that the cancer is breast cancer renders the rejection moot. Applicant has also submitted a declaration by inventor Reed, discussing the invention with regard to prostate cancer. Applicant's arguments filed 8-16-2000 have been fully considered but they are not persuasive.

Applicant has not limited the claims to the enabled scope, nor addressed the art which teaches in direct contradiction to the instant invention. As set forth in the previous office action, and reiterated above, the teachings of the art are contrary to the instantly claimed invention. The art teaches that in breast cancer, over expression of BAG-1 correlates with poor prognosis and decreased survival, which is contrary to the instant claims. Applicant has not addressed this

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discrepancy by argument or by amendment. Applicant's limitation of the scope to breast cancer fails to overcome this rejection. With regard to applicant's declaration, the declaration describes a single type of cancer where increased levels of BAG are associated with increased risk of tumor recurrence. The disclosure fails to teach this association, or to address the relationship of BAG levels to prostate cancer at all. Therefor, as set forth in the previous office action with regards to claims 16-37 and 44-45, and newly applied to claims 1-15, 38-43, and 46-49, there is insufficient support under 35 USC 112 first paragraph for the full scope of the claims.

5. The rejection of claim 23 as containing subject matter which was not properly described in the specification is maintained for reasons set forth in the previous office action.

Applicant argues that the specification does not teach the in vitro standards are unreliable, but that in vitro cultured cells can be used for result reference. Applicant's arguments filed 8-16-2000 have been fully considered but they are not persuasive.

As set forth in the previous office action, the specification provides no guidance that in vitro reference levels allow relative determination of BAG expression in cells. The support cited by applicant is a mere suggestion that BAG expression reference level might be derived from in vitro cultured cells. There is not evidence that this in fact correlates to BAG expression levels. Further while applicant has stated that the specification does not teach that in vitro cultured cell results are not unreliable, applicant has submitted no argument so or evidence to support this contention, absent the mere suggestion that in vitro results might be used.

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6. The rejection of claim 47 as containing subject matter which was not properly described in the specification is maintained for reasons set forth in the previous office action.

Applicant argues by citing a section of the specification, claiming that one of skill in the art, with the aid of the guidance in the specification could determine treatment efficacy based on BAG expression levels. Applicant's arguments filed 8-16-2000 have been fully considered but they are not persuasive.

As set forth in the previous office action, the guidance and objective evidence presented in the instant specification are insufficient to enable claims which are drawn to determining treatment efficacy. The guidance in the specification teaches how one might determine treatment efficacy, but provides no evidence or guidance that BAG might correlate to said efficacy, and if it does, what BAG levels correlate to what prognosis.

7. The rejection of claims 48-49 as containing subject matter which was not properly described in the specification is maintained for reasons set forth in the previous office action.

Applicant argues by citing a section of the specification, claiming that one of skill in the art, with the aid of the guidance in the specification could determining^e the prognosis of disease free survival or overall survival. Applicant's arguments filed 8-16-2000 have been fully considered but they are not persuasive.

As set forth in the previous office action, the guidance and objective evidence presented in the instant specification are insufficient to enable claims which are drawn to determining the

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prognosis of disease free survival or overall survival. The guidance in the specification teaches a theoretical method as to how one might determine treatment the prognosis of disease free survival or overall survival, but provides no evidence or guidance that BAG actually does correlate to said prognosis of disease free survival or overall survival.

8. The rejection of claims 1, 3-4, 6-11, 13-15, 42-43, and 45-46 under 35 USC 102(b) as being anticipated by Zapata et al. is maintained for reasons of record.

Applicant argues that Zapata et al. fails to teach a method for determining prognosis of disease free or overall survival, citing specifically a section where Zapata et al. teaches that how BAG functions in pathogenesis and progression remains to be determined. Applicant's arguments filed 8-16-2000 have been fully considered but they are not persuasive.

The section of Zapata et al. cited by applicant teaches that how BAG functions remains to be determined, but does not question BAG's correlation to prognosis, which was set forth by statistically significant test results. As set forth in the previous office action, Zapata et al. teaches that there is a statistically significant correlation between BAG-1 immunostaining an invasive cancer, which is known to have a poorer prognosis. Determination of how BAG-1 functions is not commensurate in scope with the claims.

9. The rejection of claims 1, 3-4, 6-15, 38-43, and 45-46 under 35 USC 103(a) as being anticipated by Zapata et al., in view of Sano et al. is maintained for reasons of record.

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Applicant's arguments regarding Zapata et al. Are addressed supra. Applicant further argues that Sano et al. fails to overcome the deficiencies of Zapata et al. Applicant's arguments filed 8-16-2000 have been fully considered but they are not persuasive.

This argument is rendered moot, as set forth above, since the rejection over Zapata et al. has been maintained.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Nichols, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [anthony.caputa@uspto.gov].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that sensitive information could be identified or exchanged unless the record includes a properly

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signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Jennifer Nichols, Nee Hunt

November 19, 2000

Brenda Brumback
BRENDA BRUMBACK
PATENT EXAMINER